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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/526,193	03/15/2000	Michael R. Hayden	50110/002005	9414

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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/02/2002 21

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/526,193	HAYDEN ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *184-186,188-190 and 192-194* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *159 and 160* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 September 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continuation of Disposition of Claims: Claims pending in the application are 135,136,142-145,147-151,156-163,165,166,168,169,172-176,178-181,184-190,192-194 and 213-225.

Continuation of Disposition of Claims: Claims rejected are 135,136,142-145,148,149,151,156-158,161-163,165,166,168,169,172-176,178-181 and 213-225.

DETAILED ACTION

Application Status

Claims 135, 136, 142-145, 147-151, 156-163, 165, 166, 168, 169, 172-176, 178-181, 184-190, 192-194, and 213-225 are pending in the application.

Amendment to claims 135, 136, 138, 142-145, 149, 158-16163, 165-169, 172-176, 179, 181, 184, 188, 189, 193, and 194, cancellation of claims 112-134, 137, 139-141, 146, 152-155, 164, 170, 171, 177, 182, 183, 191, 195, and 196 and addition of claims 197-212 in Paper No. 19, filed 09/11/02, is acknowledged.

Amendment to claims 135 and 166, cancellation of claims 138, 167, and 197-212, and addition of claims 213-225 in Paper No. 20, filed 10/11/02, is acknowledged.

Receipt of formal drawings in Paper No. 18, filed 09/11/02, is acknowledged.

Applicants' arguments filed in Paper No. 19 and 20 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Newly submitted claims 184-186, 188-190, 192-194 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: regarding claims 184-186 and 188, the claims are drawn to a process for identifying a compound that modulates cholesterol levels in a mammal and, regarding claims 189, 190, and 192-194, these claims are drawn to a process for identifying a compound that modulates ABC1 expression. These processes are distinct from the originally presented claims drawn to methods of identifying ABC1 modulators as the processes of claims 184-186, 188-190, 192-194 are independent as they comprise different steps, utilize different products and/or yield different results.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 184-186, 188-190, and 192-194 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Due to the significant number of claims and amendments to said claims, the examiner requests that applicants provide a copy of all pending claims in the response to this Office action.

Interview Summary

1. A telephonic interview was conducted on 10/03/02. Examiners Steadman, Prouty, and Applicant Grant discussed the following issues regarding the amendment to claims filed in Paper No. 19. The examiners suggested focusing the invention to overcome the outstanding rejections. As an example, the examiners suggested amending claim 135 to limit the human ABC1 polypeptide to a human ABC1 polypeptide comprising amino acids 1-60 of SEQ ID NO:1 in order to overcome the outstanding art rejections. Applicants inquired as to whether the argument and amendment presented in Paper No. 19 would overcome the written description rejection of claim 143 under 35 USC 112, first paragraph. The examiners indicated that no decision had been made as to this matter. The examiners agreed that the argument and amendment pertaining to claim 143 would be fully considered at a later time. Applicant also inquired as to whether claim 189 would be considered a separate invention. The examiners indicated the matter was still under consideration. While applicants expressed a desire to expedite the prosecution of the case by "phone prosecution", the examiner is of the opinion that the outstanding issues would be best addressed in a formal written Office action.

Drawings

2. The drawings have been reviewed and are objected to by the draftsperson. See the attached "Notice of Draftsperson's Patent Drawing Review" (Form PTO 948) for details.

Claim Objections

3. Claim 181 is objected to because of the following informalities: the term "claims 143" is grammatically incorrect and should be replaced with, for example, "claim 143". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

4. Claims 135, 136, 142, 161-166, 168, 169, 172-176, 178, 184-186, and 188 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 135 (claims 136 and 142 dependent therefrom), 161 (claims 162-165 and 174 dependent therefrom), 166 (claims 168 and 175 dependent therefrom), 169 (claims 172 and 173 dependent therefrom) are unclear because the claim is drawn to "[a] process for identifying a compound that modulates mammalian ABC1... ...comprising contacting a compound with a human ABC1" (underline added). It is unclear as to whether a compound that modulates ABC1 hydrolysis or binding of ATP will also modulate all mammalian ABC1 polypeptides. It is suggested that applicants clarify the meaning of the claim.

6. Claim 172 is confusing in the recitation of "process of claim 169 membrane". The examiner can find no recitation of the term "membrane" in claim 169. It is suggested that applicants clarify the meaning of the claim.

7. Claim 176 (claim 178 dependent therefrom) is incomplete as it is unclear as to whether the "mutant hABC1 polypeptide" has ABC1 biological activity and the scope of biological activities that are being measured for modulation. One of skill in the art would recognize that mutations to a polypeptide's amino acid sequence may result in a non-functional polypeptide. Thus, it is unclear as to how a skilled artisan would detect a difference in biological activity. Furthermore, it is unclear as to what biological activities are being measured for modulation.

8. Claim 176 is indefinite as it is unclear as to the the mutant hABC1 biological activity that is being screened. From the claims and

9. Claim 184 (claims 185 and 186 dependent therefrom) is confusing in the recitation of "following said thereby" in line 4. It is suggested that applicants clarify the meaning of the claim.

10. Claims 168 and 188 are indefinite as being dependent upon cancelled claims 167 and 182, respectively. Claim 167 was cancelled in Paper No. 20 and claim 182 was cancelled in Paper No. 19. It is suggested that applicants correct the claim dependency so that the claim is dependent upon a pending claim.

Claim Rejections - 35 USC § 112, First Paragraph

11. The written description rejection of claims 135, 136, 142, 161-163, 165, 166, 168, 169, and 172 under 35 U.S.C. 112, first paragraph, is withdrawn. The amendment to the claims limits the genus of ABC1 polypeptides to a human ABC1 polypeptide comprising amino acids 1-60 of SEQ ID NO:1. The recited genus of human ABC1 polypeptide comprising amino acids 1-60 of SEQ ID NO:1 is sufficiently described in the specification. The source of the genus of human ABC1 polypeptides is identified as being human, the activity of the polypeptide is identified as being ABC1 biological activity (defined in the specification at page 15, lines 10-14), and a structure common to all members of the recited genus of human ABC1 polypeptides is recited, i.e., amino acids 1-60 of SEQ ID NO:1. There is no indication in the specification that the recited human ABC1 polypeptide comprising amino acids 1-60 of SEQ ID NO:1 is intended to encompass mutants or variants of a human ABC1 polypeptide, and thus, the recited genus of human ABC1 polypeptides comprising amino acids 1-60 of SEQ ID NO:1 is limited to those that are naturally-occurring.

12. The written description rejection of claims 143-145, 148, 149, 151, 156-158, 176, 178-181, and 213-225 under 35 U.S.C. 112, first paragraph, is maintained. The rejection was fully explained in previous Office actions. Applicants exhaustively argue (beginning at page 12 of Paper No. 19) the structures of the recited genus of mammalian ABC1 polypeptides need not be disclosed in the specification. Specifically,

applicants argue the claims are directed to methods of identifying ABC1 modulating agents using assays of ABC1 biological activities and that such activities would be expected to be similar from one animal to another. Applicants argue the discovery of the ABC1 activity of lipid transport is a physiological process of an ABC1 protein. Applicants argue that ABC1 functionality is all that is required to practice the claimed assay and that the sequences of the species of ABC1 polypeptides encompassed by the recited genus are not required. Applicants argue the examiner's reliance on *UC California v. Eli Lilly*, (43 USPQ2d 1398) is misplaced as the claims of *UC California v. Eli Lilly* were directed to genetic material. Applicants argue the instant claims are not directed to ABC1 polypeptides, but to assays of these polypeptides for identifying modulators of their activity and one does not need the structures of these polypeptides to practice the invention. Applicants arguments are not found persuasive.

It is acknowledged that the claims are directed to methods of identifying modulators of mammalian, mouse, or human ABC1 polypeptides and not to mammalian, mouse, or human ABC1 polypeptides themselves. However, the recited polypeptides are an essential feature of the claimed invention and therefore, require adequate written description in the specification. Based on the specification and the prior art, it appears that a human ABC1 polypeptide having N-terminal amino acids 1-60 was not conventional in the art or known to one of skill in the art. The specification discloses that human and mouse ABC1 polypeptides having an additional 60 amino acids at the N-terminus were not known (see pages 40 and 41 of the instant specification) and that based on studies using an antibody specific for an antigen in this 60 amino acid region, it appears that this region is present and conserved among human, mouse, and chicken ABC1 polypeptides (see pages 50 and 51 of the instant specification). Furthermore, applicants suggest that the previously unreported N-terminal amino acids 1-60 may be important in the function of the ABC1 polypeptide (page 51 of the specification), particularly in the transport of cholesterol (page 38 of the specification), which was not an assigned function of a human ABC1 polypeptide at the time of the invention (see page 19, top, of Paper No. 19). Therefore, an ABC1 polypeptide comprising amino acids 1-60 at the N-terminus of the polypeptide appears to an essential

element of the claimed invention, necessary for the functioning of ABC1-mediated lipid transport as assayed for in the processes of the claims.

Furthermore, the specification does not provide a representative number of species of mutant human ABC1 polypeptides sufficient to adequately describe the genus of mutant human ABC1 polypeptides. As stated above, while the claims are not directed to the mutant human polypeptides themselves, the recited genus of mutant human ABC1 polypeptides is an essential feature of the claimed invention and therefore, requires adequate written description in the specification. A representative number of species of the recited genus of mutant human ABC1 polypeptides should be provided such that a skilled artisan would recognize that applicants were in possession of the claimed invention. The rejection is maintained for the reasons of record and the reasons described above.

13. The scope of enablement rejection of claims 135, 136, 142, 161-163, 165, 166, 168, 169, and 172 under 35 U.S.C. 112, first paragraph, is withdrawn. The amendment to the claims limits the scope of ABC1 polypeptides to a human ABC1 polypeptide comprising amino acids 1-60 of SEQ ID NO:1. The scope of recited human ABC1 polypeptides comprising amino acids 1-60 of SEQ ID NO:1 is fully enabled by the specification. As previously stated, the source of the polypeptide is identified, i.e., human, the activity of the polypeptide is identified, i.e., a biological activity of an ABC1 polypeptide defined in the specification at page 15, lines 10-14, and a structure common to all members of the recited genus of ABC1 polypeptides is recited, i.e., amino acids 1-60 of SEQ ID NO:1. There is no indication in the specification that the recited human ABC1 polypeptide comprising amino acids 1-60 of SEQ ID NO:1 is intended to encompass a broader scope of human ABC1 polypeptides such as mutants or variants of a human ABC1 polypeptide. Thus, the recited genus of human ABC1 polypeptides comprising amino acids 1-60 of SEQ ID NO:1 is limited to those that are naturally-occurring.

14. The scope of enablement rejection of claims 143-145, 148, 149, 151, 156-158, 176, 178-181, and 213-225 under 35 U.S.C. 112, first paragraph, is maintained. The rejection was fully explained in previous Office actions. Applicants argue (beginning at page 16 of Paper No. 19) the scope of recited ABC1 polypeptides is fully enabled by the specification. Regarding the outstanding rejections, applicants

reassert their arguments related to the written description rejection as summarized in item 12 above. As such, the examiner will not reiterate applicants' arguments. Applicants' argument is not found persuasive.

The specification does not support the claimed invention because of the broad scope of mammalian, human, and mouse ABC1 polypeptides or mutant human ABC1 polypeptides as recited in the claims. It is acknowledged that the claims are directed to methods of identifying modulators of mammalian, mouse, or human ABC1 polypeptides and not to mammalian, mouse, or human ABC1 polypeptides themselves. However, even though the prior art provides sequences of human, mouse, and chicken ABC1 polypeptides, the scope of recited polypeptides is not enabled by the specification. Based on the specification and the prior art, it appears that a mammalian, particularly human, ABC1 polypeptide having N-terminal amino acids 1-60 was not conventional in the art or known to one of skill in the art. The specification discloses that human and mouse ABC1 polypeptides having an additional 60 amino acids at the N-terminus were not known (see pages 40 and 41 of the instant specification) and that based on studies using an antibody specific for an antigen in this 60 amino acid region, it appears that this region is present and conserved among human, mouse, and chicken ABC1 polypeptides (see pages 50 and 51 of the instant specification). Furthermore, applicants suggest that the previously unreported N-terminal amino acids 1-60 may be important in the function of the ABC1 polypeptide (page 51 of the specification), particularly in the transport of cholesterol (page 38 of the specification), which was not an assigned function of a human ABC1 polypeptide at the time of the invention (see page 19, top, of Paper No. 19). Therefore, one of skill in the art would not have been able to practice the claimed invention with *any* mammalian, human, or mouse ABC1 polypeptide. A mammalian, human, or mouse ABC1 polypeptide comprising amino acids 1-60 at the N-terminus of the polypeptide would be essential for assaying for inhibitors of lipid transport.

Also, as stated above, while the claims are not directed to the mutant human polypeptides themselves, the scope of recited mutant human ABC1 polypeptides is not enabled by the specification. It is well known in the art that a single or multiple mutations in a polypeptide's amino acid sequence can significantly alter a polypeptide's function. Therefore, one of skill in the art would have recognized the

unpredictability of generating any single mutation or a combination of mutations in a polypeptide with an expectation of obtaining the desired biological activity. Therefore, the expectation that the claimed processes can be practiced following the guidance provided in the specification is highly unpredictable and would require undue experimentation. Thus, Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The rejection is maintained for the reasons of record and for the reasons discussed above.

Claim Rejections - 35 USC § 102

15. Rejections of claims 139 and 141 as being anticipated by Luciani et al. (IDS reference; EMBO J 15:226-235, 1996), rejection of claims 161-163 and 165 as being anticipated by Becq et al. (IDS reference; *J Biol Chem* 272:2695-2699, 1997), and rejection of claims 161, 164, and 166-168 as being anticipated by Hamon et al. (IDS reference; *Blood* 90:2911-2915, 1997) are withdrawn. None of the cited references teaches or fairly suggests an ABC1 polypeptide, either human or mouse, comprising amino acids 1-60 of SEQ ID NO:1. Therefore, the methods of claims 139, 141, and 161-168 would not be anticipated by any of the cited references.

Claim Rejections - 35 USC § 102/103

16. Rejection of claims 135 and 137 are rejected as anticipated by or, in the alternative, obvious over Luciani and rejection of claims 136 and 140 are rejected as anticipated by or, in the alternative, obvious over Becq are withdrawn. As stated above, none of the cited references teaches or fairly suggests an ABC1 polypeptide, either human or mouse, comprising amino acids 1-60 of SEQ ID NO:1. Therefore, the methods of claims 135-137 and 140 would not be anticipated or rendered obvious by references of Luciani or Becq.

Claim Rejections - 35 USC § 103

17. Rejections of claims 138 and 142 as being unpatentable over Luciani in view of Hamon, rejection of claim 164 as being unpatentable over Becq, rejection of claim 165 as being unpatentable over Hamon, rejection of claims 169-171 as being unpatentable over Becq in view of Hamon, rejection of claim 172 as being unpatentable over Becq in view of Hamon as applied to claims 169-171 and further in view of GenBank Accession Number AJ012376 and Blom et al., rejection of claims 189, 190, and 192-194 as being unpatentable over Hamon in view of GenBank Accession Number AJ012376, are withdrawn. As stated above, none of the cited references teaches or fairly suggests an ABC1 polypeptide, either human or mouse, comprising amino acids 1-60 of SEQ ID NO:1. Therefore, the methods of the claims would not be rendered obvious by the cited references.

Conclusion

18. Claims 135, 136, 142, 143-145, 148, 149, 151, 156-158, 161-163, 165, 166, 168, 169, 172-176, 178-181, and 213-225 are rejected.

19. Claims 159 and 160 are objected to as being dependent upon a rejected base claim.

20. Claims 184-186, 188-190, and 192-194 are withdrawn from consideration.

21. Claims 135, 136, 142, 143-145, 148, 149, 151, 156-160, 161-163, 165, 166, 168, 169, 172-176, 178-181, and 213-225 would be allowable if rewritten to overcome the objection(s) and/or rejection(s) under 35 U.S.C. 112, first and second paragraphs, set forth in this Office action.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally

be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600